REMARKS

Claims 74, 77-80, and 82-93 are under examination in this case. These claims stand rejected under 35 U.S.C. § 112, first and second paragraphs, and 35 U.S.C. § 102(b). Each of these issues is addressed below.

Amendments

Claims 88, 90, and 91 have been amended to incorporate the language of claim 74 and are now presented as independent claims. The preamble of these claims has also been amended to require that the claimed reduction in antigenicity be relative to wild-type AAV, an amendment that finds support in the specification, for example, at page 5, line 29 and within the claims. Claims 94-98 are newly added; these claims find support in original claims 80 and 82-85, which are now canceled. These amendments add no new matter.

For the record, Applicants do not agree with the present rejections and reserve the right to pursue all canceled subject matter without prejudice in a later filed continuation application.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 74, 77-80, and 82-93 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. The bases for this rejection are addressed below.

Claim 74 stands rejected because of the term "reducing the antigenicity of an AAV particle" and the assertion that the metes and bounds of the term cannot be determined without a definition. The Office asserts that it is unclear how one would measure antigenicity and that, in the absence of additional method steps, there are no clear endpoints for "reduction." Claim 74 has been canceled, but this language is now incorporated into independent claims 88, 90, and 91, and their dependent claims. As applied to these claims, the rejection is respectfully traversed.

The Office is first directed to Applicants' specification at page 5, line 23 to page 6, line 35, where this claim language is defined. There, it is stated clearly that what is meant by reducing the antigenicity of an AAV particle is any reduction in AAV-mediated antibody production and/or antibody binding in a host. Further, the specification, at this passage, indicates that the endpoint to be achieved is a reduction in antigenicity relative to wild-type AAV. The specification also provides a number of exemplary assays for measuring antigenicity leading to either a humoral or cellular immune response. Further, the preamble of all claims has been amended to require that the reduction in antigenicity be "relative to wild-type AAV." This basis for the rejection may be withdrawn.

Claims 89, 92, and 93 also stand rejected under 35 U.S.C. § 112, second paragraph. These claims have been canceled, and the rejection as applied to these claims is therefore moot.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 74, 77-80, 82-90, 92, and 93 stand further rejected, under 35 U.S.C. § 112, first paragraph as failing to satisfy the written description requirement. As applied to the current claims, this rejection is respectfully traversed. The rejection turns on the assertion that "The claims are drawn to a method of reducing the antigenicity of an AAV particle, wherein the modifications to the VP1-3 include a large genus of modifications. The claims encompass any modification (deletion, substitution, replacement, addition, etc.) at any point in the VP1-3 regions." This rejection should be withdrawn. As amended, Applicants' claims specify particular sites within the AAV structural proteins that are modified and further specify what type of modification is to be made. Further, each of these modifications is described in Applicants' specification. Claims 88, 90, and 91, as well as new claims 94-98, satisfy the written description requirement.

Rejection under 35 U.S.C. § 102(b)

Claims 74, 77-80, and 82-93 stand further rejected under 35 U.S.C. § 102(b) as being anticipated by Mamounas *et al.* (WO 97/38723). This rejection is respectfully traversed on a number of grounds.

First, the present claims are directed to a method for *reducing the antigenicity of AAV* by introducing at least one recited modification into an AAV structural protein. The claims further require that the modified structural protein form AAV particles and that the AAV having the modified structural protein retain infectivity. Nowhere is this claimed invention disclosed by Mamounas. As indicated previously, Mamounas does not disclose a mutated AAV structural protein that is capable of supporting viral particle formation, as required by the claims, and Applicants continue to assert that the current claim language distinguishes the claims from Mamounas. The present claims require that it is the "*modified* structural protein" that "*forms AAV particles*" and that "the AAV *having* the *modified* structural protein *retains infectivity*." These claim requirements specify that it is the *modified capsid protein* (not a protein encoded by a second or third plasmid construct) that must be capable of forming the viral particles and that it is the AAV *having* that modified capsid that retains infectivity. Contrary to the position taken by the Office, the use of the term "comprising" elsewhere in the claims does not change or negate this requirement, and, on this basis alone, the rejection should be withdrawn.

Moreover, the Office further bases the current rejection on the assertion that "The deletion [of Mamounas] results in reduced specificity of the virus for the AAV receptor (page 4, lines 22-26), which is a reduction of the antigenicity of the virus for its natural receptor." This statement is incorrect. Reduction in antigenicity, as required by the claims, refers to reduction in a host antibody response or antibody binding interaction with the AAV particle, and not to the interaction of the virus with its receptor. Mamounas does not teach that the modifications referred to by the Office reduce antigenicity, and this basis for the rejection should also be withdrawn.

Further, the claims now specify particular sites for AAV modifications, none of which is disclosed as an AAV insertion site by Mamounas. The Office indicates that "the modifications made by Mamounas are the same as those claimed by Applicant" on the basis that "some of the [Mamounas] insertions occur in the XhoI and XbaI cleavage sites (page 67, lines 21-23)" and that "Mamounas also teaches deleting a region of the VP1 or VP3 region and inserting a targeting ligand, which is an additional modification (page 4, lines 28-31)." These statements inadvertently mischaracterize the teachings of the reference.

With respect to the asserted XhoI and XbaI insertions, Applicants point out that the present claims do not include an XbaI insertion, and the teaching of such an insertion cannot anticipate the claims. Further, as indicated at page 67 of the specification, the XhoI site referred to by Mamounas is not an insertion site in the AAV sequence, but rather is a cloning site in the vector, pCDNA3, that is used in conjunction with a compatible AAV SalI site. This is illustrated in accompanying Exhibit I.

In addition, the Mamounas AAV deletions referred to by the Office do not occur at the same sites as the deletions and insertions presently claimed. The Mamounas deletions, which are summarized in Table 1 at page 61 and described at page 62, occur between nucleotides 2278-2304 ("Vp1 hydro"), 2779-2793 ("D0"), 2827-2841 ("D1"), 2854-2868 ("D2"), 2890-2904 ("D3"), and 2920-2934 ("D4") of the AAV sequence, as shown in Exhibit II. In contrast, Applicants' claims require insertions and deletions occurring between nucleotides 2310-2398 (claims 88 and 90) and at particular locations after nucleotide 2971 (claim 91). These sites therefore differ from the deletion sites disclosed by Mamounas.

Applicants request withdrawal of the § 102(b) rejection.

CONCLUSION

Applicants submit that this application is now in condition for allowance, and such action is respectfully requested.

Enclosed is a Petition to extend the period for replying to the Office action for one month, to and including December 29, 2005, and a check in payment of the required extension fee.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 28 December 2005

Karen L. Elbing, Ph.D.
Reg. No. 35,238

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045